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The Department of Defense Pharmacoeconomic Center
PEC UPDATE
September 2002, Vol. 02, Issue 6, www.pec.ha.osd.mil

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Why Evidence Based Medicine? (Editorial)

CAPT Joe Torkildson overcomes writer's block (it's horrible the way he suffered!) to discuss why health care providers are where we are professionally, and how Evidence Based Medicine might get us closer to where we might like to be.

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Highlights of the DoD P&T meetings

The Cliff Notes version returns (the full minutes are available on the DoD P&T Committee homepage if you'd "really rather read the whole thing, thank you very much...")

Key issues:

DoD P&T Executive Council Meeting (7 August 2002)

BCF changes

- *ADHD stimulant medications* - Adderall XR 10-, 20-, and 30-mg added; methylphenidate sustained release removed, methylphenidate immediate release and Concerta brand of extended release remain on the BCF. BCF listing for Concerta clarified to include 27- and 54-mg strengths
- *Added to the BCF*: insulin glargine, gabapentin, budesonide inhalation suspension (Pulmicort Respules), meloxicam
- *Added to the BCF contingent on signing of BPA agreement:*

venlafaxine extended release (Effexor XR). MTFs are NOT required to add Effexor XR to their formularies until they receive further notification.

- *Deleted from the BCF:* cimetidine
- *Clarified:* the Council reaffirmed its intent to keep Precision products as the sole blood glucose strip on the BCF. Precision QID strips are being phased out by the manufacturer. MTFs are encouraged to expeditiously transition to the new product, Precision Extra, which offers significant advancements compared to Precision QID.

Contracting Issues

- Due to expiration of the DoD contract for lisinopril (Zestril), MTFs will probably have to pay higher prices for lisinopril until a DoD/VA contract is awarded—hopefully by Nov 2002.
- Drug Classes Under Discussion
  - Angiotensin receptor blockers (ARBs) - the Council expanded authorized procurement strategies for ARBs to include a closed class contract that does not require patients to be switched from one agent to another.
  - Statins - recent labeling changes for simvastatin did not change the Council's decision to support any contracting/formulary strategy, including a closed class contract, that places at least one high potency statin on the BCF and does not require patients to be switched from one agent to another.
  - Thiazolidinediones (TZDs) - the Council expanded authorized procurement strategies for TZDs to include a closed class contract that does not require patients to be

Coming Up

The gala premiere of

RX NET

Mea Culpa

Our apologies for being late this month—waiting on the DoD P&T Committee Minutes to come out (see our summary article on Page 3) sort of had a domino effect.

Excellent Quotes of the Month

"EBM is really helpful only to those who have decided to go ahead and choose the option that at the same time serves both our patient and society. Which side are you on?"

Why Evidence Based Medicine?
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switched from one agent to another.

DoD P&T Committee Meeting (8 August 2002)

- Multiple drugs were added to the NMOP Formulary; Ritalin LA (methylphenidate extended release) was excluded from the BCF listing for methylphenidate
- 30-day quantity limits in the NMOP for antibiotics, interferon gamma, interferon alpha, sandostatin injection and testosterone transdermal patches were removed; 30-day quantity limits were retained on myeloid stimulants (except PEG-filgrastim)
- Dihydroergotamine 1 mg/ml, heparin sodium 5,000 & 10,000 units/ml, and promethazine 25 mg/ml were added to the NMOP Covered Injectables List.

Summary of Changes to the BCF and NMOP Formulary

Pretty self-explanatory, really.

Barb's Barbs: Evidence Based Medicine Links

Some of Dr. Roach's favorite EBM links. Like she says, it might even keep your patients from "biting the big one." (Dr Roach doesn't fool around with intermediate outcome measures...)

Generic Metformin

The new DoD/VA mandatory source contract for generic metformin offers at least a 85% cost reduction compared to brand name Glucophage—a potential savings of about $2 million per month.

New Drug Watch

Angela Allerman catches us up on developments in the proton pump inhibitor class (and even tries to explain the status of generic and over-the-counter omeprazole!), reviews the drugs considered at the Aug 2002 DoD P&T Committee meeting, and gives us the scoop on some other newly approved drugs, new generics, new formulations, new indications & new guidelines.

"PDTS may very well end up paying for itself many times over—while saving lives."

What is PDTS Worth? Page 8

PEC Update Information

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Would you like to receive the e-mail newsletter direct to your Inbox? Let us know by e-mailing Carol Scott, the PEC secretary, at carol.scott@amedd.army.mil.

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Submitting Articles

Do you have an article you'd like to see published in the *PEC Update*? Just send CAPT Torkildson or Shana Trice an e-mail, or call the PEC at DSN 421-1271, Commercial (210) 295-1271.

Publication Schedule

The *PEC Update* is published 10 times per year (monthly except July and December. On the

PDTS Corner

Update on the Pharmacy Data Transaction Service

What is PDTS Worth? COL (Ret) Roger Williams addresses a difficult question—placing a dollar figure against a system implemented primarily to enhance patient safety.

New PDTS Connectivity Alerts - Up till now, CHCS site managers were often unaware that PDTS connectivity had been lost until they received a call from the pharmacy or the PDTS Customer Service Support Center, since the only way sites received notification was the appearance of “UA” printed on prescription labels. Recent modifications will provide additional notification in the form of online messages, e-mails, and printouts to users of the system.

Top 10 Level 1 Drug-Drug Interactions for July 2002 by Point of Service

Top 50 Drugs for July 2002 by Point of Service

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grounds that no one is paying much attention those months, anyway...).

Errata

August 2002 PEC Update, page 4: Simvastatin Labeling Changes

The statement "the risk of muscle related adverse effects is 6% when combined with amiodarone" should have been more specific. The risk of muscle related adverse effects is reported to be 6% when *simvastatin 80 mg* is combined with amiodarone.

Our Disclaimer

The opinions expressed in this work are the views of the author(s), and do not necessarily reflect the views of the Department of Defense, the Army, Navy, Air Force, or the TRICARE Management Activity. Information presented in this work is meant for academic and educational purposes only. It is not intended nor should it be used as the definitive reference for the treatment or prophylaxis of various diseases. Use of specific product brand names are for identification purposes only unless otherwise indicated.

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EDITORIAL

Why Evidence Based Medicine?

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CAPT Joe Torkildson, MC, USN
Director, Clinical Operations Division
DoD Pharmacoeconomic Center

Editors' Letters

Please send your letters to the editors to Dr. Torkildson at Joseph.Torkildson@amedd.army.mil

I knew it would happen eventually, but I didn't expect it so soon. Writer's block is a terrible thing. I've spent a good part of the last 2 weeks sitting in front of a blank computer screen or running ideas through my mind as I drove back and forth to where ever I was going. I was trying to figure out how to make this great point about how evidence-based medicine (EBM) is key to our ability to practice medicine successfully, and how we as providers shouldn't rely on pharmaceutical company representatives to be our sole source of information regarding the medications we prescribe. And after 2 weeks I was left with about four sentences that very clearly and concisely conveyed absolutely no message at all.

It occurred to me at that point that maybe I was asking the wrong question. This is a very popular theme in the leadership portion of the MBA program that I am currently enrolled in. In their parlance, I had jumped to the "how" questions before asking the "why" questions. As a result, I was predicating my argument on some rather iffy assumptions, including the one that "all health care providers are 100% convinced of the value of EBM when seeking to provide the best possible care to patients." Yet in conversations with providers I've found ample evidence that this is not the case. I've heard enough pejorative statements ("cookbook medicine", "no accounting for experience", "waste of time") to realize that a substantial number of prescribers view this whole issue with either uncertainty, fear, anger, or even disdain. It finally dawned on me that the real question facing providers today isn't how best to implement EBM into their clinical decision-making. Instead providers are struggling with the real issue of reconciling the values they hold that lead them to medicine as a profession with the realities of medical practice in today's society. So I decided

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to let the drug reps off the hook this month, and spend some time instead considering the questions of why are we where we are as a profession, and how might EBM get us closer to where we might like to be.

So what is our calling as providers? I am going to ignore for the moment all the bad press the medical profession has gotten the past few years, the exponential growth in malpractice litigation, and our slip from the top when individuals are asked what profession they trust the most. I assert that we continue to be engaged in the noblest and most crucial profession on the face of the earth. When we are practicing our profession effectively, we not only cure patients of disease and disability, or relieve them of the physical and/or psychic pain that results from their condition; we also work cooperatively with them to maximize their wellness, happiness, and potential for self-actualization. **WOW!** Throw in a few miracles and we could all be candidates for sainthood. So why the bad press, why the lawsuits, why the fall from grace in the eyes of our patients? I would like to suggest that it is at least partly explained by the fact that we now spend so much time trying to figure out how to get our job done that we don't spend the time needed to remind ourselves why we get it done. We get so bogged down in forms and paperwork and seemingly arbitrary administrative decisions that eat up our time and limit our ability to do what we think is right, we forget to notice the tremendous rush that occurs when we realize that we've actually made a huge difference in the life of another. And even worse, the decisions we make when treating patients can become more dependent on what is least likely to get us sued than what is best both for the patient and the society in which we all live.

But what does this have to do with EBM? The Centre for Evidence-Based Medicine at the University of Oxford has developed one of the best definitions of EBM that I have come across. Their definition of EBM is: "Evidence-based medicine is the conscientious, explicit and judicious use of current best evidence in making decisions about the care of individual patients." EBM is nothing more than a tool that assists us in making those treatment decisions that we are called on to make every day. We can argue about what are the best sources of "current best evidence"; in fact, my initial editorial was going to revolve completely around my opinion that we need to dig deeper than the reprints dropped on our desk by the latest pharmaceutical rep to darken our door. But that's not the real issue. The real issue is, "What do I hope to accomplish through this encounter with this patient?" Is it to ensure that each patient receives exactly the treatment he or she needs in order to optimize both their health and the health of the larger society, or is it to decrease the likelihood by 5% that the patient will be calling back in 3 days complaining that the treatment doesn't work, even if that option costs twice as much?

EBM can be tremendously helpful in helping us decide what type of treatment best fulfills the goal stated above, identifying what is best both for our patient and for the society in which we both live. But it's of value only if we get up every morning committed to the notion that this day we will fearlessly practice our profession, that we will make the difficult decisions rather than taking the easy way out and making the decision that is least likely to require us to see the patient back, or to get us sued. Those of us who have been around for any

length of time know that these are often not the same: the right decision isn't always the safest, and the safest decision isn't always the right one. EBM is really helpful only to those who have decided to go ahead and choose the option that at the same time serves both our patient and society. Which side are you on?

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DoD P&T Highlights

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News from the 7 and 8 August 2002 meetings of the DoD Pharmacy &Therapeutics (P&T) Executive Council and the DoD P&T Committee

Shana Trice, Clinical Pharmacy Specialist
DoD Pharmacoeconomic Center

Complete minutes of the DoD Pharmacy & Therapeutics (P&T) Committee and the DoD P&T Executive Council meetings are available on the PEC website at **www.pec.ha.osd.mil/PT_Committee.htm.** The next meetings are scheduled for 20-21 Nov 2002, at the Uniformed Services University of the Health Sciences, Bethesda, MD. Items for the agenda should be submitted to the co-chairs no later than 18 October 2002.

Quick Links

DoD P&T Executive Council Meeting (7 August 2002)

BCF changes

- ADHD stimulant medications - Adderall XR 10-, 20-, and 30-mg added; methylphenidate sustained release removed, methylphenidate immediate release and Concerta brand of extended release remain on the BCF. BCF listing for Concerta clarified to include 27- and 54-mg strengths
- Added to the BCF: insulin glargine, gabapentin, budesonide inhalation suspension (Pulmicort Respules), meloxicam
- Added to the BCF contingent on signing of BPA agreement: venlafaxine extended release (Effexor XR)
- Deleted from the BCF: cimetidine
- Considered for BCF addition, but not added: aspirin/extended release dipyridamole (Aggrenox)
- Considered for BCF deletion, but not deleted: cyproheptadine, theophylline elixir

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- Clarified: status of blood glucose test strips on the BCF

Contracting Issues

- Expiration of lisinopril contract
- Generic contract awards, renewals, and terminations
- Drug Classes Under Discussion
  - Angiotensin receptor blockers (ARBs)
  - Statins
  - Thiazolidinediones (TZDs, "glitazones")
- Contract initiatives still pending: Leutinizing Hormone Releasing Hormone (LHRH) agonists, nasal corticosteroids, triptans, and quinolones

DoD P&T Committee Meeting (8 August 2002)

- Newly Approved Drugs
  - Added to the NMOP Formulary:
  - NMOP or Retail Network Formulary Restrictions:
  - BCF Clarifications:
- Uniform Formulary Proposed Rule
- Changes to NMOP Quantity Limits: antibiotics; myeloid stimulants, interferon gamma, interferon alpha, and sandostatin injection; testosterone transdermal patches
- Injectable Drugs in the NMOP
- Controlled Distribution Drugs

DoD P&T Executive Council Meeting (7 August 2002)

BCF Changes (See **Page 4** for a consolidated list of changes to the BCF and the NMOP Formulary)

Attention Deficit Hyperactivity Disorder (ADHD) stimulant medications

After reviewing the need for uniform availability of both methylphenidate and amphetamine products for ADHD; the preferability of extended release formulations; rapidly increasing use of Adderall XR and decreasing use of Adderall immediate release in the retail network; minimal use of methylphenidate sustained release in both MTFs and the retail network; and the opinions of DoD providers who treat children with ADHD, the Council made the following changes to the BCF:

- Retain Concerta (methylphenidate extended release) and methylphenidate immediate release on the BCF.
-

Remove methylphenidate sustained release from the BCF

- Add Adderall XR 10-, 20- and 30-mg strengths to the BCF. Facilities may add additional strengths if they desire, but they are not mandated to do so.

The Council also clarified the listing for Concerta to include all the currently available strengths: 18-, 27-, 36-, and 54-mg capsules. Two reasons: 1) multiple strengths allow more precise titration of dosages, and 2) a recent PEC review of Concerta utilization at MTFs noted that several large MTFs were dispensing a large number of dual prescriptions to patients for both 18-mg and 36-mg Concerta capsules rather than dispensing the 54-mg capsules—resulting in inconvenience to the patient, an increase in workload for the pharmacy, and an excess cost of $38.40 per patient per month.

Insulin glargine (Lantus) added to the BCF

The Council added insulin glargine to the BCF after concluding that it represents a true advance in the treatment of both Type 1 and Type 2 diabetes and should be uniformly available at MTF pharmacies. Considerations in favor of addition included its clinical characteristics (evidence of an approximately 10% reduction in the incidence of symptomatic hypoglycemia, nocturnal hypoglycemia, and severe hypoglycemia compared to NPH insulin, making a more aggressive approach to escalating insulin therapy possible); increasing use of insulin glargine in both MTFs and the retail network; and enthusiastic provider opinion. On the down side: insulin glargine costs much more than human NPH insulin at MTF pharmacies ($25.38 versus $4.49 per 10 ml vial) and is currently on fewer than half of MTF formularies.

Gabapentin (Neurontin) added to the BCF

The Council added gabapentin to the BCF due to its recent approval for past herpetic neuralgia; high usage across the Military Health System (usage has continued to rise in all three points of service; the majority of use appears to be for neuropathic pain in patients over 65); and the expectation that a generic version of gabapentin may become available soon (**Editor's note**: we don't know when).

Budesonide inhalation suspension (Pulmicort Respules) added to the BCF

The Council agreed with a request to add Pulmicort Respules to the BCF after considering its place in therapy (the only FDA-approved, nebulized steroid available, can be used for patients as young as 12 months of age); the prevalence of asthma among children; and the current use of this medication in the MHS (almost exclusively for patients in the 0 to 4 age group). The Council noted that MDIs are still the inhaled steroid formulation of choice in the treatment of asthma; budesonide inhalation suspension is intended for those who cannot yet use MDIs appropriately.

[**Editor's note**: An informational paper for providers on the indications for

prescribing Pulmicort Respules has been kindly provided for the *PEC Update* by Dr. Henry A. Wojtczak (CAPT, USN, MC). Dr. Wojtczak is a pediatric pulmonologist currently stationed at Naval Medical Center, San Diego. The paper is included here as a resource for MTFs that may want to produce a similar handout for their primary care providers. **Click here to download** (MS Word format).

Meloxicam (Mobic) added to the BCF

The Council added meloxicam to the BCF after extensive discussion (see the Executive Council minutes for the full write-up). The Council agreed that the evidence for a GI-sparing effect with meloxicam is not as certain as that for rofecoxib, but that there is sufficient evidence to conclude that meloxicam is associated with fewer serious GI events (perforations, obstructions, GI bleeds and/or symptomatic ulcers) than the less COX-2 selective NSAIDs with which it has been compared in clinical trials. (This conclusion was based primarily on results of large pooled analyses of clinical trial data with meloxicam rather than on the often cited SELECT and MELISSA studies, which were of too short a duration to draw any conclusions regarding the incidence of serious GI events with meloxicam.)

The manufacturer has offered DoD a blanket purchase agreement (BPA) for meloxicam. The BPA provides a price reduction from $0.89 to $0.79 for the 7.5 mg tab and from $0.98 to $0.88 for the 15 mg tab, a reduction of about 11%, in return for placing meloxicam on the BCF. The BPA would be effective no later than Oct 2002 and run through 31 Dec 2003. The BPA does not prevent later addition of a COX-2 inhibitor or any other NSAID to the BCF.

The Council emphasized that because meloxicam is still substantially more costly than generic NSAIDs (e.g., naproxen, ibuprofen, diclofenac), it does not make sense to use meloxicam in patients at low risk of GI events. The Council agreed that facility-level guidelines or programs to ensure appropriate use of meloxicam, as well as celecoxib, rofecoxib, or valdecoxib, are consistent with BCF policy as long as the guidelines are applied uniformly and consistently (e.g., to both military and civilian providers). Minutes explain that:

> "It is difficult to accurately predict whether addition of meloxicam to the BCF will result in greater cost (if meloxicam is used in place of generic NSAIDs) or cost avoidance (if meloxicam is used in place of celecoxib, rofecoxib, or valdecoxib). One large Army MTF that previously had celecoxib and rofecoxib on formulary with a criteria-based prospective medication use evaluation form deleted celecoxib and rofecoxib from their formulary and added meloxicam after discovering that a majority of the patients receiving celecoxib or rofecoxib did not meet criteria. After 4 months, they reported substantial cost avoidance, no adverse drug reactions, no new drug requests for celecoxib or rofecoxib as a result of treatment failures, and a 100%

conversion rate when outside providers were contacted requesting a change to meloxicam."

The Council also considered addition of etodolac to the BCF, but decided that it did not have sufficient data and tabled the issue to a later date.

Venlafaxine extended release capsules (Effexor XR) added to the BCF—contingent on the signing of a blanket purchase agreement

The Council added venlafaxine extended release 37.5-, 75-, and 150-mg tablets to the BCF, contingent on the signing of a BPA between Wyeth-Ayerst and DSCP formalizing a verbal offer of a $0.10 per tablet price reduction on the 150-mg tablet. MTFs are **NOT** required to add venlafaxine extended release to their formularies until they receive further notification.

Assuming the BPA is signed, this decision closes an item pending since Feb 2002, when the Council first concluded that venlafaxine extended release was useful in the treatment of several anxiety disorders, particularly in patients with co-morbid depression, and was a candidate for addition to the BCF. The Council concluded that the MHS would likely realize a small immediate cost avoidance from the BPA and *might* avoid additional cost if BCF addition facilitates MTF recapture of venlafaxine extended release prescriptions from the retail network.

Cimetidine deleted from the BCF

The Council agreed with a MTF provider's request to delete cimetidine from the BCF because its indications and efficacy are similar to ranitidine (which is on the BCF); cimetidine has more side effects and drug interactions; the majority of MTF H2 blocker prescriptions are for ranitidine; and ranitidine costs less.

Aspirin/extended release dipyridamole (Aggrenox) NOT added to the BCF

The Council turned down a request to add aspirin/extended release dipyridamole (Aggrenox) to the BCF. Considerations included: minimal usage of Aggrenox in DoD; lack of support by primary care providers (20 of 25 respondents were against BCF addition); lack of conclusive evidence of a significant advantage over the concomitant use of aspirin and dipyridamole to reduce the risk of stroke; and lack of a clear benefit over clopidogrel, which is already on the BCF.

Cyproheptadine remains on the BCF

An MTF pharmacist requested deletion of cyproheptadine from the BCF because of low usage and because there are better alternatives for treating allergies and headache on the BCF. The Council decided not to remove cyproheptadine from the BCF after more than 90 responses were received from providers and pharmacists in the field citing cyproheptadine's unique place in therapy (there are no good alternative treatments for pregnant patients

and young children with migraine headaches), as well as its low cost (as low as $0.03 per 4-mg tablet).

Theophylline elixir remains on the BCF

An MTF pharmacist requested deletion of theophylline oral liquid from the BCF based on low usage at the requestor's MTF. The Council decided not to remove theophylline oral liquid from the BCF after noting that the the oral liquid form is the only dosage form that is suitable for some patients (i.e., children and elderly patients, who may not be able to swallow solid dosage forms or use a metered-dose-inhaler effectively). The Council noted that while usage of theophylline has greatly decreased, it remains on asthma and COPD treatment guidelines.

Status of blood glucose test strips on the BCF clarified

A medical/surgical product standardization initiative for TRICARE Regions 6, 7 and 8 recently selected the Accucheck (Roche Diagnostics) blood glucose test strip. Some pharmacies were incorrectly told that they had to switch from the Precision test strip (which is on the BCF) to the Accucheck test strip.

The Council reaffirmed its intent to keep Precision products as the sole blood glucose strip on the BCF. Precision (Abbott) blood glucose test strips have been on the BCF since its inception. Precision's status on the BCF is supported by an incentive price agreement that offers a lower price system-wide as market share increases.

The Council noted that Abbott Diagnostics plans to phase out the Precision QID strip and meter, while phasing in their newer product, Precision Extra, which offers significant advancements over the Precision QID

Requests to delete particular strengths or dosage forms of BCF items

The Health Affairs Policy for Basic Core Formulary and Committed Use Requirements Contracts (Policy #98-034) states, “In the case of multiple strength BCF drugs, all strengths need not be stocked but all prescriptions for that agent will be filled regardless of strength.” The BCF page on the PEC website explains that a listing for an oral medication “indicates all oral dosage forms and strengths will be provided unless otherwise noted.”

The DoD P&T Executive Council has deleted or excluded some dosage forms/strengths from the BCF for one or more of the following reasons:

- Substantially higher cost than other dosage forms/strengths
- Excessive administrative burden associated with maintaining multiple strengths (e.g., controlled substances)
- The BCF listing is intended to cover an indication that is limited to a specific dosage form/strength (e.g., fluconazole 150 mg for vaginal yeast infections)
- New dosage form/strength offers no significant clinical advantage and is apparently designed to avert competition from generic versions of the drug
- Low usage combined with one or more of the

product. The Council encourages MTFs to expeditiously transition to the Precision Extra product.

(**Editor's Note:** LCDR Ted Briski is the PEC point of contact for questions regarding blood glucose test strips. His articles in the **May** and **August** 2002 editions of the *PEC Update* provide additional information and contact information.)

factors above

Some MTF requests to delete a particular strength or dosage form of a BCF drug appear to be based primarily on objections to stocking an item that has a low usage rate. The Council reiterated that if an MTF has little or no demand for a particular BCF item, the MTF is not required to physically stock the item in the pharmacy. However, the MTF must provide the item if it is prescribed.

Contracting Issues

Expiration of lisinopril contract

The DoD contract for the Astra-Zeneca brand of lisinopril (Zestril) expired 31 Jul 02; the VA's contract for the Merck brand of lisinopril (Prinivil) expires 19 Oct 02. Both Astra-Zeneca and Merck are phasing out production of lisinopril. DoD and VA are seeking a joint contract for a generic version of lisinopril, to be awarded after the VA's Prinivil contract expires. Generic versions of lisinopril are not yet listed on the Federal Supply Schedule and all are priced significantly higher than the previous DoD contract price of $0.14 per tablet. MTFs will probably have to pay higher prices for lisinopril until the DoD/VA contract is awarded—hopefully by Nov 2002.

Contract Awards, renewals, and terminations

- **New contracts awarded:** benztropine, carbidopa/levodopa IR, famotidine, digoxin, indomethacin, metformin, captopril, paclitaxel, trazodone, and chlorhexidine.
- **Contracts not awarded** because the bid prices were higher than existing FSS prices: prednisone and cimetidine.
- **In various stages of solicitation:** penicillin, dicloxacillin, tretinoin cream, amoxicillin, and cephalexin.
- **Renewed:** salsalate and all Geneva generics

See **DSCP's DMM-Online website** for a **complete list of DoD and DoD/VA contracts, including contract prices and NDCs**. Questions regarding DoD and joint DoD/VA contracts may be directed to MAJ John Howe at DSCP or LCDR Ted Briski at the PEC.

Angiotensin Receptor Blockers (ARBs)

After reconsidering its earlier decision not to support a closed class contract for ARBs, the Council concluded that while its concerns about therapeutic interchangeability and clinical coverage for treating congestive heart failure and preventing the progression of renal disease in type 2 diabetics remain, a closed class contract would be acceptable because the usage of ARBs for these conditions is low enough that MTFs could use the non-formulary request process to provide non-contracted ARBs to these patients if necessary. The Council expanded the authorized procurement strategies for the ARBs to include a closed class contract that does not mandate that patients be switched from non-contracted ARBs to the contracted ARB. The decision clears the way for DoD to potentially join the VA in seeking a closed class contract for an ARB.

Use of ARBs in DoD

An analysis of data from the Uniformed Services Prescription Database (USPD) and the M2 database found ICD-9 codes consistent with a diagnosis of CHF or type 2 diabetic renal disease for only 289 (5%) of 5,680 patients who were prescribed two or more daily doses of an ARB. Patients with CHF are more likely to be prescribed multiple daily doses of an ARB than patients who are being treated for hypertension.

Statins

After reviewing recent changes to the label for simvastatin (Zocor; Merck) that further clarifies the risk of myopathy and rhabdomyolysis (particularly with higher doses of simvastatin and when used with other drugs), the Council concluded that the label change is not cause to alter its previous decision to support any contracting/formulary strategy (to include a closed class contract) that places at least one high potency statin on the BCF and does not require patients to be switched from one agent to another. The Council noted that myopathy and rhabdomyolysis are well-known side effects of all statins and that the label changes were voluntarily initiated by the manufacturer as a result of normal post-marketing surveillance and monitoring of ongoing clinical trials.

The Council also noted that a recent **Clinical Advisory on the Use and Safety of Statins** from the **National Heart, Lung, and Blood Institute**, the **American College of Cardiology**, and the **American Heart Association** states that a review of

Labeling changes for simvastatin include:

- *Concomitant use with fibrates and niacin (> or = 1g/day)* – simvastatin dose should not exceed 10 mg daily unless the benefit outweighs the increased risk.
- *Concomitant use with amiodarone or verapamil* – simvastatin dose should not exceed 20 mg daily unless the benefit outweighs the increased risk. In a clinical trial, 6% of patients taking amiodarone and simvastatin 80 mg daily developed myopathy. Combined clinical

data regarding reports of fatal rhabdomyolysis among the different statins strongly suggests that there are no clinically important differences in the rate of fatal complications among the five statins now available in the U.S., and that clinicians should consider the rates of severe myopathy as equivalent among these statins.

trial data showed a 0.6% risk of myopathy with simvastatin (20-80 mg) and verapamil.

- *Dose-related risk of myopathy / rhabdomyolysis* – the incidence in clinical trials, in which patients were carefully monitored and some interacting drugs were excluded, has been approximately 0.02% at 20 mg, 0.07% at 40 mg & 0.3% at 80 mg.

Updated package labeling is available from the manufacturer at **www.zocor.com**.

Thiazolidinediones (TZDs)

After reconsidering its May 2002 decision that any procurement strategy for TZDs must leave the TZD class "open" on the BCF, the Council expanded the authorized procurement strategies for the TZD class to include a closed class contract that does not mandate that patients be switched from a non-contracted TZD to a contracted TZD. The decision was primarily based on 1) results of a more extensive analysis of changes in LDL-C levels (incremental to placebo) reported in clinical trials of TZDs, and 2) an analysis of concomitant statin therapy for DoD patients who were newly started on TZD therapy. (**Editor's Note:** see minutes for summaries of both analyses.) While the data from clinical trials suggest that rosiglitazone is associated with larger increases in LDL-C than pioglitazone, concomitant usage of statins by DoD patients is very similar for both drugs. The decision clears the way for DoD to potentially join the VA in seeking a closed class contract for a TZD.

DoD P&T Committee Meeting (8 August 2002)

Newly Approved Drugs – See the New Drug Watch article on **Page 7** of this issue of the *PEC Update* and Appendix A of the **Aug 02 DoD P&T Committee minutes** for more information on the drugs.

Added to the NMOP Formulary - Voriconazole 50- and 200-mg tablets (Vfend; Pfizer); etonogestrel/ethinyl estradiol vaginal ring (Nuva-Ring; Organon); methylphenidate long acting capsules (Ritalin LA; Novartis); escitalopram tablets (Lexapro; Forest); Bravelle brand of urofollitropin added to NMOP Covered Injectables List, which already includes other brands of urofollitropin; dihydroergotamine 1 mg/ml injection, heparin sodium 5,000 & 10,000 units/ml injection, and promethazine 25 mg/ml injection added to NMOP Covered Injectables List; InnoLet brand of human insulin for injection (3 mL prefilled syringes) added to NMOP Covered Injectables List.

Excluded from the NMOP Formulary - Lovastatin extended-release tablets (Altocor; Andrx/Aura): existing statin contract precludes addition

BCF Clarifications - methylphenidate long acting capsules (Ritalin LA, Novartis) excluded from the BCF listing for methylphenidate; lovastatin extended-release tablets (Altocor; Andrx/Aura): existing statin contract precludes addition to the BCF (or MTF formularies)

Uniform Formulary (UF) Proposed Rule

The comment period for the UF proposed rule has closed. The TMA Pharmacy Program Office is currently in the process of formulating responses to comments submitted by the public.

Where to Find the Uniform Formulary Proposed Rule

The UF Proposed Rule has been published in the Federal Register, Vol 67, No 71, FRI 12 Apr 2002; Civilian Health and Medical Program of the Uniformed Services. (Try going to the Federal Register by GPO Access page, (**www.gpo.gov/su_docs/aces/aces140.html**), checking the boxes for Vol 67 and "proposed rules", and specifying 04/12/2002 and some or all of the term "Civilian Health and Medical Program of the Uniformed Services" in the search boxes.)

NMOP Quantity Limit Clarifications

Antibiotics

The Council eliminated the 30-day quantity limit on antibiotics in the NMOP after agreeing that providers are unlikely to prescribe large quantities of antibiotics unless the patient needs long-term antibiotic therapy. Antibiotics will be dispensed according to the general rule applied to other drugs in the NMOP (up to a 90 day supply). Existing quantity limits for specific antibiotics will remain in force. All quantity limits will be posted on the quantity limit page on the PEC website. The change should decrease the administrative burden, risk of running out of medication, and cost (number of copays) for patients with a legitimate need for long-term antibiotic therapy.

Myeloid stimulants, interferon gamma, interferon alpha, and sandostatin injection

Because literature supports chronic use of the interferons and sandostatin for specific indications, the Committee unanimously voted to remove the 30-day quantity limit from interferon alpha, interferon gamma, and sandostatin. The Committee agreed that a 30-day quantity limit on myeloid stimulants was reasonable given the products' indications and uses. They noted that the NMOP quantity limit for PEG-filgrastim was set at 2 syringes per 45-day supply at the May 2002 meeting. The Committee retained the 30-day quantity limit for myeloid stimulants, except for PEG-filgrastim, which will remain as 2 syringes per 45-day supply limit. The quantity limits will be posted on the PEC website quantity limit page.

Testosterone transdermal patches (Androderm)

Because testosterone topical gel (Androgel) has a NMOP quantity limit of 90 days and both Androgel and Androderm are chronic replacement products with low abuse potential, the Committee voted unanimously to remove the 30-day quantity limit on all topical/transdermal testosterone or androgen replacement products.

Injectable Drugs in the NMOP

Based on an analysis of prescriptions for injectable drugs being filled in the retail network, the Committee added the following drugs to the NMOP Covered Injectables List: dihydroergotamine 1 mg/ml, heparin sodium 5,000 & 10,000 units/ml, and promethazine 25 mg/ml. Because other migraine medications are subject to quantity limits and because use of dihydroergotamine should not exceed 6 ampules per week for safety reasons, the Committee established a quantity limit for dihydroergotamine: 3 boxes (30 ampules) per 30 days in the retail network and 9 boxes (90 ampules) per 90 days in the NMOP.

After noting the substantial usage and higher costs in the retail network for injectable drugs available from the NMOP, the Committee noted the opportunity for cost avoidance if the NMOP were to be used more aggressively to fill prescriptions for injectable drugs that are included on the NMOP Covered Injectables List.

Controlled Distribution of Prescription Drugs

The Committee noted that all the Managed Care Support Contractors have established network agreements with CVS Procare Specialty Pharmacy, making CVS Procare the preferred site for DoD patients to obtain drugs requiring controlled distribution. The current plan is to use CVS Procare, whenever possible, for future drugs requiring controlled distribution. Information about specific drugs is available on the PEC website. LCDR Ted Briski (**Ted.Briski@amedd.army.mil**) is the PEC point of contact for distribution issues.

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Summary of Changes to the Basic Core Formulary and National Mail Order Pharmacy Formulary

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Resulting from the 7-8 August 2002 meetings of the DoD Pharmacy & Therapeutics Executive Council and the DoD Pharmacy & Therapeutics Committee

1. BCF Changes

A. Additions to the BCF

1. Venlafaxine extended release capsules (Effexor XR) - contingent on signing of BPA
2. Insulin glargine injection (Lantus)
3. Gabapentin (Neurontin)
4. Budesonide inhalation solution (Pulmicort Respules)
5. Meloxicam tablets (Mobic)
6. D, L-amphetamine 10-, 20-, 30-mg extended release capsules (Adderall XR)

B. Deletions from the BCF

1. Cimetidine oral
2. Methylphenidate SR (sustained release) tablets removed from the BCF listing for methylphenidate

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C. Changes and clarifications to the BCF

1. The current BCF listing for methylphenidate was clarified to specify the following strengths for methylphenidate extended release (Concerta): 18-, 27-, 36-, and 54-mg
2. Existing BCF listings for Novolin insulin are for 10 ml vials. MTFs may decide whether or not to add alternative insulin delivery devices (e.g., insulin pens, InnoLet) to their formularies
3. Precision products remain the only blood glucose strips on the BCF. MTFs are encouraged to transition to the newer Precision product, Precision Extra, as soon as possible.

D. Exclusions from the BCF

1. Methylphenidate long acting capsules (Ritalin LA, Novartis) were excluded from the BCF listing for methylphenidate.
2. Lovastatin extended-release tablets (Altocor; Andrx/Aura) - existing statin contract precludes addition to the BCF (or MTF formularies)

2. NMOP Formulary Changes

(For more information see **minutes** of the 8 August 2002 DoD P&T Committee Meeting)

A. Additions to the NMOP Formulary

1. Voriconazole 50- and 200-mg tablets (Vfend; Pfizer); injectable formulation not added since it is not for self-administration
2. Etonogestrel/ethinyl estradiol vaginal ring (Nuva-Ring; Organon)
3. Methylphenidate long acting capsules (Ritalin LA; Novartis) – General NMOP rule for schedule II controlled substances for treatment of ADHD applies (90 days supply; no refills)
4. Escitalopram tablets (Lexapro; Forest)
5. Bravelle brand of urofollitropin added to the NMOP Covered Injectables List, which already includes other brands of urofollitropin
6. Dihydroergotamine 1 mg/ml injection added to the NMOP Covered Injectables List
7. Heparin sodium 5,000 & 10,000 units/ml injection added to the NMOP Covered Injectables List
8. Promethazine 25 mg/ml injection added to the NMOP Covered Injectables List
9. InnoLet brand of human insulin for injection (3 mL prefilled syringes) added to the NMOP Covered Injectables List

B. Exclusions from the NMOP Formulary -

1. Lovastatin extended-release tablets (Altocor; Andrx/Aura) – existing statin contract precludes addition to the NMOP Formulary

C. Clarifications to the NMOP Formulary - None

3. Quantity Limit Changes (NMOP and Retail Network)

1. Quantity limit for dihydroergotamine 1 mg/ml injection: 3 boxes (30 ampules) per 30 days in the retail network, 9 boxes (90 ampules) per 90 days in the NMOP.
2. NMOP 30-day quantity limit for antibiotics was eliminated. Antibiotics will be dispensed consistent with the general rule applied to all other drugs in the NMOP (up to a 90 day supply), unless otherwise specified on the quantity limit page on the PEC website.
3. NMOP 30-day quantity limits for interferon alpha, interferon gamma, and sandostatin were removed. The quantity limit for myeloid stimulants remains 30 days, with the exception of PEG-filgrastim, which has a quantity limit of 2 syringes per 45 days in the NMOP, and 1 syringe per 21 days in the retail network.
4. NMOP 30-day quantity limit for topical/transdermal testosterone or androgen replacement products was removed.

4. Changes to the Prior Authorization Program (NMOP and Retail Network) - None

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Barb's Barbs

Evidence Based Medicine Links

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LtCol Barbara Roach, USAF, MC
Air Force Medical Officer, DoD Pharmacoeconomic Center

Do the words/phrases "Boolean,""Medline search," and "Citations 1 out of 25917" make you break out in hives? That's what can happen when you need to obtain a current answer to a medical question for your patient. You certainly couldn't use the aforementioned medline search in your office (25,917 is the number of citations you will get if you simply type "hypertension" into OVID and choose Medline 1996-current). You need something simpler and quicker, or (even better) something that has already been appraised for you.

Try the following sites when you need a reliable answer in a jiffy.

EBM Search Engines – Use these **before** going to OVID or MEDLINE. (AKA let someone else find the information for you.) Both of these search engines simultaneously search multiple Internet sites and organize the results for you on a single page.

- **SUMSearch - http://sumsearch.uthscsa.edu**
- **TRIP Database - www.tripdatabase.com**

Pre-appraised EBM sites – meaning someone who knows what they're doing has done the work for you in critically assessing the articles. (They are listed in order of highest reliability of source combined with lowest work required from you.) Sometimes you want to find the information yourself.

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The Cochrane Collaboration (www.cochrane.org) is an international collaboration of health professionals having **NO** support from the pharmaceutical industry. They do systematic reviews of every paper published on a topic, regardless of the language or journal, to give a definitive answer. Biggest problem is that very current medications will not be covered yet since each systematic review takes about 2 years to complete. Produces the **Cochrane Library - www.update-software.com/cochrane** - OVID carries this; otherwise it is "for pay." Abstracts can be **browsed and searched** for free if you don't have access to OVID.

Clinical Evidence (**www.clinicalevidence.com**) is a fairly new publication (about 3½ years old) produced jointly by the **British Medical Journal (BMJ)** and the **American College of Physicians (ACP)**. Reviews **all** known systematic reviews, meta-analysis, randomized controlled trials and other evidence to answer primary care providers' common clinical questions. Gives you the information, rates the evidence, lets you make your mind up. This will soon be an Internet-only publication as they continually update **every** question they have ever dealt with in **each** issue.

This is becoming the gold standard for determining evidence-based data. Currently about $119.00/year (published twice a year in June and December). Health care professionals can still get a free copy courtesy of the United Health Foundation by going to their website at **www.unitedhealthfoundation.org** then clicking on the Clinical Evidence Button. You can then go to the "About Clinical Evidence" section and scroll down to "submit your request" or go to the "mailing list" section and fill out the information. Either way, you'll get a free copy. If you fill it out after June, you won't get your first issue until December. Copies of *Clinical Evidence Concise*, *Clinical Evidence Pediatrics*, and *Clinical Evidence Mental Health* are now being distributed in the USA, courtesy of the United Health Foundation. All recipients are also entitled to free online access to the full text. Go register!

Bandolier (www.jr2.ox.ac.uk/bandolier/index.html)- Bandolier is the monthly EBM newsletter for Oxford University, where EBM all started. This site is very entertaining and free.

ACP Journal Club (www.acpjc.org) - Like the Cochrane Library, there is also a charge associated with this site, but some of the current and archived issues are available free.

POEMS and its search engine, INFOPOEMS - The actual POEMS (Patient Oriented Evidence that MatterS) are available in the Journal of Family Practice every month. See the website at **www.jfponline.com** for information on subscribing to the Journal of Family Practice (physicians in active practice registered with the American Medical Association as general or family practitioners or primary care physicians registered with the American

Osteopathic Association can sign up for free.). The "for pay" search engine for POEMS can be found at **www.medicalinforetriever.com/index.cfm**. It's very impressive for speed, and can be downloaded onto a handheld PDA. If want a free trial, go to the INFOPOEMS website and email them via the "contact us" button. This is an excellent tool to use at the bedside/exam table.

UpToDate (**www.uptodate.com**) is a very useful but also very expensive pre-appraised EBM product. Updated quarterly. A product of 7 (so far) different medical societies.

PedsCCM Evidence-Based Journal Club (http://pedsccm.wustl.edu/EBJournal_club.html - there's an _ hidden in the underline). A free site focusing on critical reviews of clinical trials pertinent to the practice of pediatric critical care. Reviews can be downloaded onto a PDA.

Sites where you can learn EBM and how to critically appraise a journal article – for those who don't trust anyone else

Evidence Based Medicine CD Rom from the DoD/VA Clinical Practice Guidelines group - . Don't ask me why, but go to to the Army MEDCOM Quality Management Office site (**www.cs.amedd.army.mil/qmo/Home.htm**) and click on Practice Guidelines in the left hand margin and choose TUC from the drop-down list, then go to Tool Kit in the left hand margin and choose Order Form from the drop-down list. You'll see the last item is CD ROM "Evidence Based Medicine" and it's a whole course on CD ROM going through how to appraise the literature, do the common statistical calculations, etc. If you're not Army, call the contact person and they'll mail you one.

Bandolier (**www.jr2.ox.ac.uk/Bandolier**) is the most entertaining place to learn most all of these terms. The British have a way with words. Choose Bandolier Knowledge, then EBM Stories.

The original Users' Guides to Evidence-Based Practice articles from JAMA are available from Sheffield University's Netting the Evidence site (**www.shef.ac.uk/~scharr/ir/userg.html)** or from the Centre for Health Evidence (**www.cche.net/usersguides/main.asp**) and unfortunately these will bore you to sleep. Both sites have useful lists of definitions and links and other materials. Visit **www.shef.ac.uk/~scharr/ir/netting/** for Sheffield University's online freebie course on EBM, databases and much more.

Randomized Controlled Trials—A User's Guide (www.bmjpg.com/rct/contents.html) is written by Dr. Jadad from McMaster's University. He has the whole book freely downloadable or you

can purchase it from BMJ. This book teaches you how to appraise the literature. The whole reason he's done this is to show the major journals that, just like the BMJ, you **DON"T** need to charge for your journal online. Someone will still buy it. He insists that medical information be free to all professionals that need the information.

Go Forth & Do Good Things

Now that you have these sources, a lot of them for no charge; well what are you still reading this for? Get out there and make good decisions at the point of care. It should add some leisure time to your life and possibly even keep your patients from biting the big one.

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Generic Metformin

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Tom Bolinger
Data Administrator
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A DoD/VA mandatory source contract for metformin 500-, 850-, and 1000-mg tablets awarded to Caraco Laboratories became effective 5 Aug 2002. The contract provides about a 85-88% reduction in cost relative to brand name Glucophage—of great importance because of the large volume of metformin used by MTFs (about 73 million tablets per year). Notably, the contract prices for the Caraco generic also represent a significant decrease in cost even when compared to the average cost per tablet paid by MTFs for the most commonly used generic brand, Eon, which costs about $0.11 to $0.13 per tablet.

Contract NDCs and Prices for Generic Metformin (Caraco Labs)					Comparison to brand name Glucophage	
Strength	Package size	NDC	Cost per package	Cost per tablet	Average price per tablet paid by MTFs for brand name Glucophage (July 2002)	Percent Reduction
500 mg	100's	57664-0397-88	$4.50	$0.045	$0.30	-85%
	1000's	57664-0397-18	$41.00	$0.041		
850 mg	100's	57664-0435-88	$6.83	$0.068	$0.55	-88%
	1000's	57664-0435-18	$62.00	$0.062		
1000 mg	100's	57664-0474-88	$8.20	$0.082	$0.58	-86%

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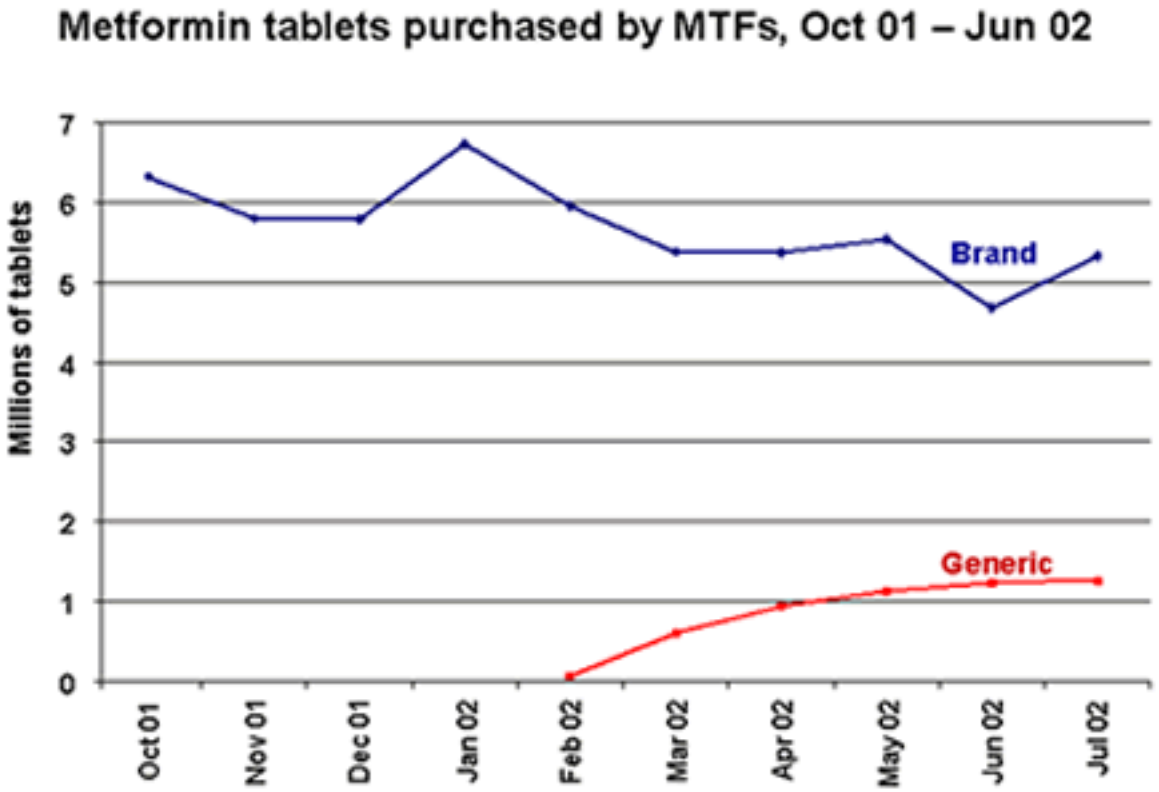
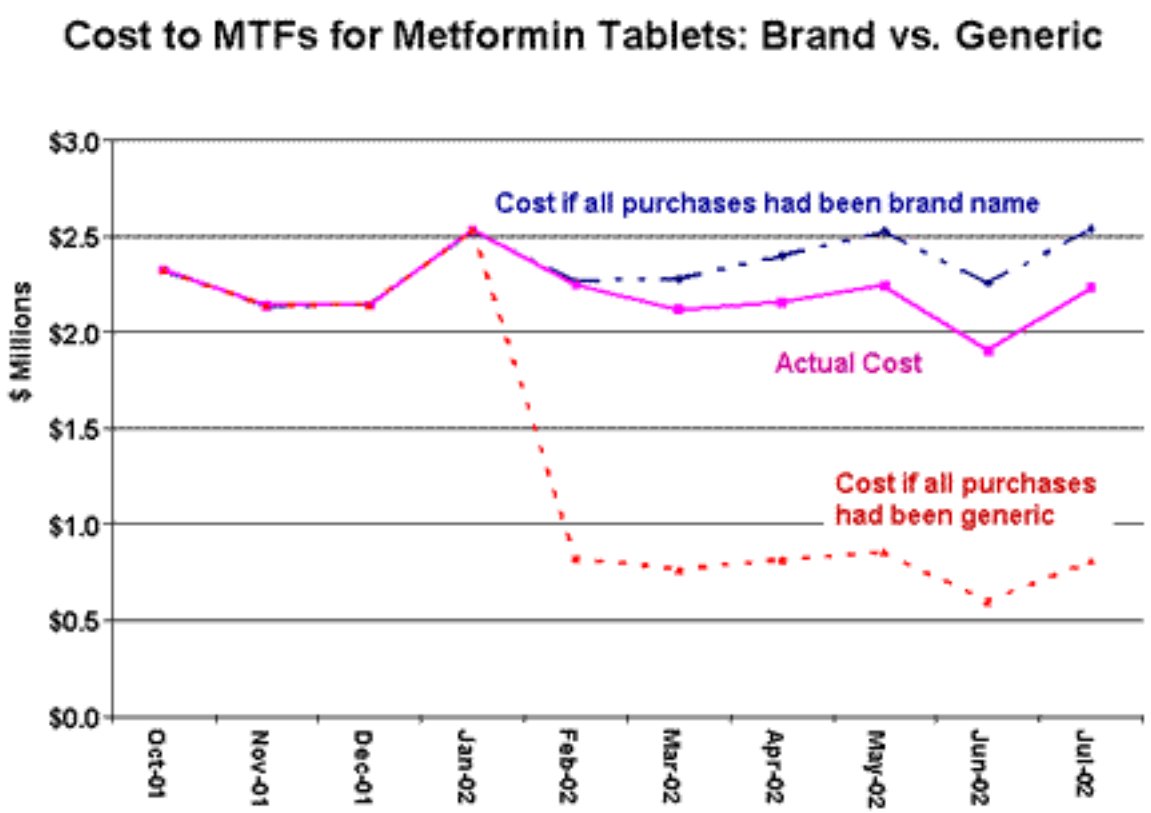
	1000's	57664-0474-18	$74.00	$0.074		

Although generic metformin has been available for some time, MTFs do not appear to be rapidly switching away from the brand name product (see tables below). As of 31 July 2002, Glucophage still held 81% of the market by tablets purchased—and MTFs spent about $1.4 million more during July 2002 than they would have had they purchased the most commonly used generic. The second table below shows graphically 1) what would have been spent by MTFs if all purchases were for the brand name only, 2) what was actually spent, and 3) what would have been spent if all purchases had been for generic metformin. The price per tablet used for these calculations was for the generic most commonly purchased by MTFs during this time period (Eon). (It is worth noting that prices paid for generic products can vary widely—a few MTFs appear to have paid more per tablet for particular brands of generic metformin than they would have for brand name Glucophage.)





The potential cost avoidance becomes even more marked when contract prices are figured into the equation: **based on the number of metformin tablets purchased in Jul 02, the potential reduction in cost with 100% utilization of the contract product is at least $2 million per month—$24 million per year.**

Whether or not generic use could really have reached 100% in July is unknown, since there could well have been difficulties in ordering or obtaining lower priced generic products. In addition, MTFs may have been waiting for results of the contracting initiative before making a change. With the contract now in place, however, there's no reason not to take advantage of it! MTFs should be sure to let their prime vendors know what their requirements are (see CDR Brian Kerr's response to this very question in the Aug 2002 *PEC Update*) and notify DSCP of any difficulty in obtaining the contracted product.

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Proton Pump Inhibitors - the Saga Continues

With both generic and over-the-counter versions of omeprazole on the horizon, this situation is getting confusing!

Over-the-Counter Omeprazole - Just when you thought things couldn't get any more complicated, there is now a new twist to consider. Proctor & Gamble received an "approvable" designation from the FDA on 22 Aug 02 for an OTC omeprazole formulation (Prilosec 1). In contrast to prescription Prilosec, which is a capsule, Prilosec 1 is a tablet containing 20.6 mg of the salt omeprazole magnesium. The OTC tablet will be indicated for "prevention of the symptoms of frequent heartburn"; the recommended duration of therapy is 14 days, after which consumers are advised to consult a physician. This narrow indication differs from indications for the prescription formulation, which is labeled for use in GERD, duodenal ulcer, hypersecretory conditions like Zollinger-Ellison and Barrett's esophagus, and gastric ulcer. Because their indications differ, prescription omeprazole products will continue to be marketed even after Prilosec 1 becomes available. OTC omeprazole could be available by the 1st half of 2003, pending revision and testing of the product label to made sure consumers can understand it.

Generic Omeprazole - Verdicts in pending patent infringement cases are expected in the near future. If AstraZeneca loses, Andrx is likely to be the first generic company to market omeprazole since it was the first generic to be approved by the FDA (pending

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resolution of patent issues) and therefore has 180 days of marketing exclusivity.

Rabeprazole - The voluntary FSS price reduction for rabeprazole (Aciphex) will expire 31 Dec 02. Representatives from Janssen have informed the PEC that **the price for rabeprazole will increase** after that date; it is unknown what the new price will be. New information will be sent out to the field via established e-mail channels and published in the *PEC Update* as it becomes available.

Table 1: DoD Prices for Proton Pump Inhibitors as of 15 Aug 2002

Generic	Brand	Dose	Current Price per Tab/Cap
Rabeprazole	Aciphex	20 mg	$0.22 (FSS)*
Lansoprazole	Prevacid	30 mg	$0.99 (BPA) $2.24 (FSS)
Pantoprazole	Protonix	40 mg	$0.90 (FSS)
Omeprazole	Prilosec	20 mg	$2.08 (FSS)
Esomeprazole	Nexium	20 mg	$2.43 (FSS)

FSS = Federal Supply Schedule prices as of 15 Aug 02;
BPA = Blanket Purchase Agreement
* Voluntary price reduction expires 31 Dec 2002

Drugs Discussed at the August 2002 DoD P&T Meetings

Five newly approved drugs were discussed at the August 2002 DoD Pharmacy and Therapeutics Committee meeting. None of these drugs were added to the BCF.

A new azole antifungal agent for invasive aspergillosis & serious fungal infections in patients intolerant or refractory to other therapy

Voriconazole (Vfend, Pfizer) is an azole antifungal agent approved for treating invasive

aspergillosis primarily caused by *Aspergillus fumigatus* and for treating serious fungal infections caused by *Scedosporium apiospermum* and *Fusarium spp* in patients intolerant of or refractory to other therapy. It is available in both injectable and oral formulations. Use of this drug is expected to be limited to bone marrow transplant patients, AIDS patients, or other immunocompromised patients. The most significant limitation of voriconazole is its drug interaction profile with medications metabolized by the CYP450 system. Voriconazole was not added to the BCF. Voriconazole oral tablets were added to the NMOP Formulary. The injection must be given IM and is not suitable for self-administration; it will not be available from the NMOP.

A novel contraceptive formulation

Etonogestrel / ethinyl estradiol vaginal ring (Nuva-Ring, Organon) is a self-inserted vaginal ring indicated for pregnancy prevention. The ring remains in place for 3 weeks, followed by a 1-week break for withdrawal bleeding. The estrogen/progestin components have a controlled-release mechanism, which provides a more uniform hormonal concentration compared to the oral contraceptives, but it is unknown whether this translates into tolerability benefits. Since the active ingredients are released vaginally, hepatic 1st-pass metabolism is avoided, allowing for lower steroid doses. Nuva-Ring has the same safety precautions as the oral contraceptives, and similar efficacy. Nuva-Ring was added to the NMOP Formulary.

A new extended release methylphenidate for Attention Deficit Hyperactivity Disorder (ADHD)

Methylphenidate extended release capsule (Ritalin LA, Novartis) is a new once-daily formulation for children with ADHD aged 6-12 years. Ritalin LA provides an immediate release of methylphenidate and a second delayed release of methylphenidate approximately 4 hours later, similar to two immediate release tablets taken 4 hours apart. Other extended release methylphenidate products include Metadate CD (which also has a duration of about 8 hours) and the BCF selection Concerta (which has a longer duration of about 12 hours). For children with swallowing difficulties, Ritalin LA capsules can be opened up and sprinkled over applesauce. The current BCF listing for methylphenidate was revised to exclude Ritalin LA. Ritalin LA was added to the NMOP Formulary; like other Schedule II drugs for the treatment of ADHD, up to a 90-day supply may be obtained from the NMOP (no refills).

A new SSRI (well, in a way): the active isomer of citalopram

Escitalopram (Lexapro, Forest) is the 6th SSRI on the market and the 5th to be indicated for depression. This drug was discussed at the 8 Aug P&T meeting even though the drug was not formally approved by the FDA until 14 Aug 02. Escitalopram is the S-isomer formulation of citalopram (Celexa), which is a racemic mixture of R- and S-isomers. The single isomer is thought to be the only one contributing to citalopram's antidepressant activity. To the extent that R-citalopram contributes to adverse effects or interferes with the action of s-citalopram, escitalopram may prove to have minor advantages compared to the racemic product; the clinical impact of any such advantage remains to be seen. Escitalopram was added to the NMOP Formulary. The Council tabled the question of whether or not to add escitalopram to the BCF (which already includes citalopram, fluoxetine, paroxetine, and sertraline) to a later date, since the drug was not yet FDA-approved at the time of the meeting.

A new extended release formulation of lovastatin

Lovastatin extended release tablets (Altocor, Andrx) have a higher bioavailability (190%) than lovastatin immediate release, allowing for a lower statin dose to achieve the same LDL effect (e.g., 80 mg lovastatin = 60 mg Altocor). Altocor won't be available commercially until Sep 2002, following expiration of the exclusivity rights of other lovastatin formulations. Altocor was not added to the BCF or NMOP formulary; the current statin contract precludes addition of other statin formulations to either formulary.

Other Newly Approved Drugs

The following newly approved drugs were only briefly discussed at the P&T Committee meeting since NMOP or BCF status was not at issue for various reasons (e.g., line extension of existing product, injectable formulations not suitable for self-administration, drugs with restricted drug distribution programs that cannot be supplied through the NMOP).

Desloratidine orally disintegrating tablets (Clarinex Redi-tab; Schering) for treating allergy symptoms and chronic idiopathic urticaria

Fulvestrant IM injection (Faslodex; Astra Zeneca) for the treatment of hormone-receptor positive breast cancer in postmenopausal women

Human insulin (rDNA origin) SC injection (InnoLet; Novo Nordisk), a novel insulin delivery system (3 mL disposable, biodegradable syringes) containing Novolin 70/30, NPH, or regular insulin. The product will be available through the NMOP.

Treprostinal injection (Remodulin; United Therapeutics) is a continuous SC infusion for the treatment of primary pulmonary hypertension with NYHA class II-IV symptoms. It is only available under a restricted drug access program.

Urofollitropin SC injection (Bravelle; Ferring), a fertility agent, was added to the NMOP Covered Injectables List, which already contains other brands of urofollitropin.

Ziprasidone IM injection (Geodon IM; Pfizer) is indicated for treating acute episodes of paranoia and schizophrenia. It was not added to the NMOP Covered Injectables List or considered for the BCF because it is not suitable for self administration and is only used emergently.

New Generics

Nifedipine 90 mg (generically equivalent to Adalat CC 90 mg) is now available from Teva Pharmaceuticals. Generic versions of 30-mg and 60-mg tablets of Adalat CC have been available from Bioavail since Dec 2000.

Enpresse (Barr Labs) triphasic oral contraceptive levonorgestrel/ethinyl estradiol - equivalent to Triphasil and Tri-Levlen.

Clarification: Amoxicillin / clavulanate (Augmentin) is available from Geneva, however, there is a supply problem, which is expected to persist until early 2003.

Clarification: A generic version of ciprofloxacin tablets has been approved by the FDA, however a recent court ruling means that generic ciprofloxacin won't be launched until Dec 2003.

New Indications

Valsartan (Diovan; Novartis) obtained FDA approval as a second line agent for CHF on 14 Aug 02, based on the 5000-patient Valsartan Heart Failure Treatment (Val-HeFT) study. Labeling states that valsartan is indicated for treating CHF in "patients who are intolerant of ACE inhibitors."

Darbepoetin alfa (Aranesp; Amgen) is now approved for treating chemotherapy-induced anemia in patients with nonmyeloid malignancies. It was originally approved in September 2001 for treatment of anemia associated with chronic renal failure in dialysis and non-dialysis patients.

New Formulations & Dosage Strengths

Synthetic conjugated estrogens (Cenestin; Barr Labs) is now available in 0.3 mg tablets. It is also available in tablets of 0.625-, 0.9- and 1.25 mg.

Amlodipine / benazepril (Lotrel; Novartis) has recently received approval for a new higher once-daily dosage strength capsule, 10/20 mg.

Significant Drugs Likely to Lose Patent Protection in the Next Few Years

**Note: projected dates are based on lists from pharmacy publications and may be little more than "best guesses." Patent litigation often alters timelines. No guarantees! **

2002
loratadine

2003
methylphenidate extended release (specifically Concerta)
nefazodone (Serzone)
quinapril (Accupril)
fosinopril (Monopril)
Ortho-Novum 7/7/7

2004
citalopram (Celexa)
fluticasone (Flonase, Flovent)
etodolac (Lodine XL)
benazepril (Lotensin)
Ortho-Tricyclen
Fluconazole (Diflucan)
Metformin/glyburide (Glucovance)
Metformin extended release (Glucophage XR)
Glipizide extended release (Glucotrol XL)

2005
ondansetron (Zofran)
lansoprazole (Prevacid)
paroxetine (Paxil)
enoxaparin (Lovenox)
ramipril (Altace)
carvedilol (Coreg)
clarithromycin (Biaxin)
glimepiride (Amaryl)

2006

pantoprazole (Protonix)
sertraline (Zoloft)
pravastatin (Pravachol)
simvastatin (Zocor)
azithromycin (Zithromax)
cefprozil (Cefzil)
pioglitazone (Actos)

Bupropion HCl sustained release tablets (Wellbutrin SR; GlaxoSmithKline) has a new 200 mg strength, in addition to existing 100 and 150 mg tablets.

New Guidelines

There has been an update to selected topics in the diagnosis and management of asthma from the National Asthma Education and Prevention Program. (**www.nhlbi.nih.gov/guidelines/asthma/index.htm**)

The International AIDS Society has published new HIV treatment guidelines (**www.iasusa.org/event/index.html#treatment_guidelines**, and **http://jama.ama-assn.org/issues/v288n2/ffull/jst20002.html**)

A new practice guideline for the diagnosis and treatment of Group A streptococcal pharyngitis is available from the Infectious Disease Society of America (**www.journals.uchicago.edu/IDSA/guidelines**)

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September 2002, Vol. 02, Issue 6, www.pec.ha.osd.mil

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Update on the Pharmacy Data Transaction Service

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What is PDTS Worth?

By COL (Ret) Roger Williams, PDTS CSSC Clinical Support Supervisor

A common way to evaluate benefits derived from a new system is to compare the costs of a given outcome before and after the new system is implemented. Unfortunately, it is very difficult to place a dollar figure against a system that was implemented primarily to enhance patient safety by reducing the risk of medication errors (in the form of drug-drug interactions and therapeutic duplications) through a prospective drug utilization review (ProDUR) process.

For the one-year period 1 Jul 01 to 30 Jun 02, PDTS identified 37,140 potential Level 1 drug-drug interactions—contraindicated drug combinations that are potentially life-threatening. More often than not, these potential drug interactions would not have been known to the provider or the pharmacist prior to the implementation of PDTS—not just because the Department of Defense's three pharmacy points of service (MTFs, NMOP, retail network) had no mechanism for interacting with each other, but also because none of the 105 MTF host clusters were able to communicate with each other.

About 10% of prescriptions causing a warning message are reversed, either prior to or shortly after the prescription is filled. Since the PDTS screens patient profiles starting 180 days prior to

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the date new medications are prescribed, a significant number of false positive warning messages probably occur; thus while a 10% reversal rate is not unrealistic, it is also unlikely to reflect the percent of prescriptions which would have resulted in an adverse drug event if filled.

According to a study conducted by the Advisory Board Committee, adverse drug events (ADEs) top the list of causes of medical errors. The study estimates the average cost of an ADE to be $4,700 per hospital admission. If we use that dollar amount as the basis for analysis, we see that PDTS has the potential to generate significant cost avoidance just from the identification of potential Level 1 drug-drug interactions. For example, if we assume 25 % (971) of the 3,883 potential level 1 drug-drug transactions that were reversed during this time period would have resulted in an ADE and a hospital admission, the cost avoidance would be $4.6 million for the year. On the other hand, if we assume that only 1% of reversed transactions (39) would have resulted in an ADE and a hospital admission, the cost avoidance would be $183,300 per year. The actual cost avoidance is likely to fall somewhere in between—we'll probably never know.

Remember that these numbers don't include indirect costs to the patient or the system (e.g., lost productivity), intangible costs (pain and suffering), or costs associated with ADEs that don't result in a hospital admission. In addition, the analysis doesn't address the potentially large cost benefits to DoD associated with the availability of a reliable source of prescription data across the entire military health system.

But most importantly, what if just one of those potentially life-threatening interactions avoided as a result of the ProDUR warning supplied by PDTS would have otherwise resulted in a patient’s death? How much cost would be avoided in this situation (a difficult question)? PDTS may very well end up paying for itself many times over—while saving lives.

New PDTS Connectivity Alerts

The loss of PDTS connectivity has always been a concern both to CHCS users and the PDTS Customer Service Support Center (CSSC). While it doesn’t occur frequently, loss of connectivity can be an issue since providers will not receive on line PDTS ProDUR warning messages that result from potential drug-drug interactions or therapeutic duplications. However, sites still receive local CHCS warnings. Once PDTS connectivity is restored, sites receive any backlog of warning messages via e-mail and the notification printer.

Up to now, the only form of notification that PDTS connectivity had been lost was the appearance of “UA” printed on the prescription labels. As a result, CHCS site managers were often unaware that PDTS connectivity had been lost until they received a call from the pharmacy or the CSSC. Recent modifications to the CHCS software to correct this problem are now being deployed. Without getting into all the technical details, the following will occur when PDTS connectivity is lost:

“UA” will still be printed on prescription labels

An on-line OPCOM message and audible bell will be sent to CHCS users with

operator privileges

An e-mail message will be sent to a MailMan e-mail group

The e-mail message will be printed to each pharmacy's PDTS Notification Printer

If you see any of these "alerts", you should contact your systems personnel immediately.

Pharmacy personnel may want to contact their CHCS site managers to insure that the procedures listed in the Implementation Update Guide: PDTS Hibernation/Flow Control/ Unavailability Alerts CHCS S/W Version 4.630 have been followed completely. As a reminder, the routine **"EN^INHPSAM"** must be run to properly activate the new transceiver. If you have any questions, please feel free to call the CSSC.

Top 10 Level 1 Drug-Drug Interactions by Point of Service

By COL (Ret) Roger Williams, PDTS CSSC Clinical Support Supervisor

The feature in PDTS that enhances patient safety is the process of conducting Prospective Drug Utilization Reviews (ProDURs). PDTS conducts on-line ProDURs (clinical screens) on all medications dispensed, regardless of the DoD point of service the patient used to have the prescription filled. Pharmacy personnel need to be aware that with the activation of PDTS, the number of clinical screenings could increase depending on how frequently patients use multiple prescription sources. PDTS clinical screens are performed only on those medications the patient obtains from outside of the dispensing site's host cluster. It will not duplicate clinical warnings generated from within the CHCS host system.

For further information about the PDTS DURs, see **my article in the Mar 2002 PEC Update**.

Top 10 Potential Level 1 Drug-Drug Interactions in MTFs, Jul 2002

Rank	Medications involved	#
1	Ibuprofen / Ketorolac tromethamine	269
2	Ketorolac tromethamine / Naproxen	119
3	Nitroglycerin / Sildenafil citrate	77
4	Ketorolac tromethamine / Rofecoxib	59
5	Isotretinoin/Minocycline HCl	49
6	Celecoxib / Ketorolac tromethamine	48

7	Doxycycline hyclate/ Isotretinoin	25
8	Itraconazole / Simvastatin	25
9	Ketoconazole / Simvastatin	25
10	Aspirin / Ketorolac tromethamine	24

Top 10 Potential Level 1 Drug-Drug Interactions in the Retail Network, Jul 2002

Rank	Medications involved	#
1	Ibuprofen / Ketorolac tromethamine	90
2	Nitroglycerin / Sildenafil citrate	64
3	Ketorolac tromethamine / Naproxen	47
4	Isotretinoin / Minocycline HCl	42
5	Celecoxib / Ketorolac tromethamine	39
6	Ketorolac tromethamine / Rofecoxib	36
7	Entacapone / Selegiline HCl	32
8	Ketoconazole / Simvastatin	30
9	Aspirin / Ketorolac tromethamine	27
10	Itraconazole / Simvastatin	24

Top 10 Potential Level 1 Drug-Drug Interactions in the NMOP, Jun 2002

Rank	Medications involved	#
1	Nitroglycerin / Sildenafil citrate	63
2	Celecoxib / Ketorolac tromethamine	19
3	Ketoconazole / Simvastatin	14
4	Amiodarone HCl / Gatifloxacin	10
5	Ketorolac tromethamine / Rofecoxib	10
6	Amiodarone HCl / Moxifloxacin HCl	8
7	Gatifloxacin / Sotalol HCl	8
8	Atorvastatin calcium / Ketoconazole	7
9	Entacapone / Selegiline HCl	7
10	Isosorbide mononitrate / Sildenafil citrate	5

Top 50 Drugs for July 2002 by Point of Service

By Preston Hardy, PDTS CSSC Clinical Support Coordinator, ACS

One of the many benefits of PDTS is the capability to review and compare prescription utilization by point of service. This month's issue continues our reports on the top 50 drugs (by prescription count) in each MHS point of service for July 2002. Click on the link below to download the file (in MS Excel format):

July 2002 MHS Top 50 Drugs by POS

The first three tables in the files list the Top 50 drugs by prescription count dispensed at MTFs, the retail network, and the NMOP. Column headings are defined as follows:

- **Drug Description** - contains all strengths and dosage forms
- **Ranking** - from 1 (most dispensed) to 50 (least dispensed)
- **# of Rxs** - number of prescriptions dispensed
- **Qty. Disp.** - total quantity of measured units dispensed
- **Avg. Qty Per Rx** - average number of measured units per prescription
- **Avg. Days Supply** - average days supply issued per prescription
- **Unique Utilizers** - number of patients receiving a prescription for the listed drug from that point of service during the reporting period in question.

The fourth table compares the Top 50 drugs in MTFs against the same drugs in the retail network and NMOP. A blank cell means that the corresponding drug did not fall in the top 50 for that specific point of service. As in the previous tables, this comparison is based on prescription count.

We are currently unable to run comparisons of all points of service by **dollars** rather than prescription count due to the fact that CHCS does not send MTF prescription cost data to PDTS.

The PDTS Customer Service Support Center

The PDTS CSSC strives to provide world-class customer support to all Military Health System users while enhancing the operational effectiveness and ensuring the quality of information maintained within the Pharmacy Data Transaction Service. The PDTS CSSC comprises the Pharmacy Benefit Operations Division of the PEC and is co-located with the Clinical Operations Division of the PEC at Ft. Sam Houston, TX.

The PDTS CSSC has an e-mail address for questions, comments, concerns, or report requests:

PDTS@cen.amedd.army.mil

Drop us an e-mail! We will respond via e-mail or call you within 1 business day.

Or call the PDTS CSSC at:

- DSN: 471-8274
- Toll-free commercial:
  1-866-275-4732
  (1-866-ASK4PEC)
- Local commercial (San Antonio):
  (210) 221-8274
- OCONUS:
  (AT&T access code)+866-275-4732

Need more information?

Many materials pertaining to PDTS, including trouble call procedures, the PDTS Report Request Form, business rules, and interchange control documents (ICDs), are available in the PDTS section of the PEC website. Just go to **www.pec.ha.osd.mil/pdts/pdts_documents.htm** and browse through the options on the left-hand navigation bar.

In addition, many articles on various aspects of PDTS and the PDTS CSSC have been published in recent issues of the *PEC Update*. Please visit the PEC Update page on the PEC website - **www.pec.ha.osd.mil/ac03000.htm** - for back issues.

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